REMARKS

Claims 1-2 and 4-5 have been rejected as being obvious under 35 U.S.C. § 103(a), over U.S. Patent # 4,758,424; issued July 19, 1988; to Denick *et al.* (hereinafter "Denick") in view of Japanese Patent JP 64007786 issued May 18, 1964; to Aida (hereinafter "Aida"). Claims 1-6 have been rejected as being obvious over International Application WO 96/22762; published August 1, 1996; in the name of Kupper (hereinafter "Kupper") either alone or in view of U.S. Patent #5,663,415; issued September 2, 1997; to Chopdekar *et al.* (hereinafter "Chopdekar"). Claims 15-30 have been rejected as being obvious over Kupper either alone, or in view of Chopdekar in further view of U.S. Patent #5,164,398; issued November 17, 1992; to Sims *et al.* (hereinafter "Sims").

Claims 1-2 and 4-5 Are Not Obvious Over Denick In View of Aida

Claims 1 and 4 are respectively directed to a composition and a method for treating cough, wherein the active ingredients consist of carbetapentane tannate and guaifenesin. Claims 2 and 5 are respectively dependent upon claims 1 and 4, and add tablet form claim elements thereto.

The Examiner argues that it would obvious to combine *guaifenesin*—taught by Denick as being a chewable cough tablet—with carbetapentane tannate—taught by Aida as being a non-irritant cough suppressor—insofar as each reference indicates that its respective active is used for "cough." The Examiner further asserts (ostensibly relying upon this single "cough" commonality) that the artisan of ordinary skill would be motivated to combine these actives owing to an expectation that the combination would

give rise to an "additive effect."

Thus, the Examiner asserts an infirm "obvious to try" rejection. *Infirm*, because whether a particular modification / combination might be "obvious to try" is not a legitimate test of patentability. In re Geiger, 815 F.2d 686, 688 (Fed. Cir. 1987). The Examiner has cited no motivation in either reference, or within the knowledge generally available to those of skill in the art, upon which to base her "additive effect" theory.

Additionally, by focusing solely on the commonality of the word "cough" for her motivation makeweight, the Examiner fails to consider the teachings of either prior art reference *as a whole*. When the teachings of the references *are* considered *as a whole* the artisan would clearly be discouraged from making the proposed combination.

Denick, *as a whole*, is directed to magnesium aluminum silicate adsorbates that are useful in masking the bitter taste of certain medicaments:

"SUMMARY OF THE INVENTION

> **A procedure for preparing a good tasting medicament adsorbate** which may contain up to about 30% by weight medicament compound has been unexpectedly discovered.
>
> This has been achieved by sorbing a solution of medicament drug into a complex magnesium aluminum silicate to form a mass **which when dried is an essentially tasteless medicament adsorbate**." (col. 1, lines 47-51; emphasis added).

> "**The taste masking sorption effect of this invention is superior to the taste masking found when a medicament drug is adsorbed on normal complex magnesium aluminum silicate**." (col. 2, lines 38-41; emphasis added).

Additionally, Denick, *as a whole*, commends his magnesium aluminum silicate adsorbates for use with medicaments that taste bad:

> "**The medicament drug may be selected from a wide range of unpleasant tasting therapeutic agents and mixtures of therapeutic agents**. (col. 3, lines 61-63; emphasis added).

Among the specific examples of unpleasant tasting therapeutic agents that Denick specifically commends is carbetapentane *citrate*:

> "Nonlimiting illustrative categories and specific examples include:
>
> ...(c) Antitussives, such as dextromethorphan, dextromethorphan hydrobromide, noscapine, **carbetapentane citrate**, and chlophedianol hydrochloride;" (col 3, line 63 to col. 4, line 3; emphasis added).

That the artisan of ordinary skill relying on the teachings of each reference *as a whole* would **not** be motivated to make the Examiner's urged addition of Aida's carbetapentane *tannate* with Denick's teachings (*inter alia* guaifenesin) is an unavoidable conclusion, because Aida *as a whole* teaches that carbetapentane *tannate* is **not** unpleasant tasting:

> "Non-irritant, **tasteless** cough-suppressor" (emphasis added).
>
> "The product **is not bitter** and is useful as a corrigent in antitussives for children." (emphasis added).
>
> "The present inventors undertook research into various organic acid salts for the purpose of resolving said disadvantages, and the result of their investigation was the discovery that **carbeter pentane tannin acid salts are flavorless** and very difficult to dissolve in water, but can be dissolved in an alkali solution. Therefore, the carbeter pentane tannin acid salt obtained by the method of the present invention **has no harsh taste** and is easy to administer, is easily dissolved in the stomach after administration, and the effect is evident." (September 10, 2001 translation of Aida by Matt Alt, USPTO Translations Branch, emphasis added).

Indeed, Aida solves the problem of carbetapentane ***citrate's*** harsh taste by converting it to carbetapentane ***tannate***. Accordingly, the artisan of ordinary skill having studied *the whole* of Denick's teachings (i.e., how to mask the off-putting bitterness of unpleasant tasting therapeutic agents) having further studied *the whole* of Aida's teachings (i.e., carbetapentane *tannate* is not an unpleasant tasting therapeutic agent) would not be motivated to combine the claimed carbetapentane *tannate* with the claimed guaifensesin.

Therefore, claims 1-2 and 4-5 are not obvious over Denick in view of Aida.

Claims 1-6 Are Not Obvious Over Kupper By Itself, Nor In View Of Chopdekar

Claims 1 and 4 are respectively directed to a composition and a method for treating cough, wherein the active ingredients consist of carbetapentane tannate and guaifenesin. Claims 2-3 and 5-6 are dependent claims adding tablet and suspension form claim elements to each of Claims 1 and 4.

The Examiner notes that Kupper is a taste masking reference, then, ignoring that teaching, the Examiner dissects Kupper into minutiae to support her argument. To be sure, like the similar properties of the *magnesium aluminum silicate adsorbates* of Denick, *so* the ability of *aloe vera* to mask the taste of harsh active ingredients **is** the primary focus of Kupper, *as a whole.* Accordingly, *how to mask harsh tasting actives* is the teaching that the artisan would glean from Kupper.

The Examiner ignores Kupper's taste masking focus then notes that Kupper's *Example II* describes a syrup, containing, *inter alia*, dextromethophan hydrobromide (HBr) and guaifenesin. The Examiner further notes that carbetapentane is one of nine specific antitussives that Kupper cites as being useful, and concedes that Kupper does not exemplify the inclusion of carbetapentane *tannate.*

The Examiner then offers Chopdekar—a reference directed, *on the whole*, toward processes for **making** *antihistamine* tannates—noting its *Background* aside that antihistamine tannates tend to be "stable" and present few untoward "side effects." Further dissecting Chopdekar, the Examiner then notes that carbetapentane is among a Markush group of 19 *antihistamines* that Chopdekar teaches can be reacted with tannic

acid. (col. 3, lines 7). [1]

The Examiner then *deems* it obvious to substitute carbetapentane for the dextromethorphan of Kupper's *Example II*, on the basis of Kupper's teaching that each of the respective free bases is an *antitussive*, and that they therefore would be "functional equivalents." The Examiner then further posits (ignoring Chopdekar's mischaracterizing of carbetapentane as an *antihistamine*) that it would be obvious, in view of both, Chopdekar's comments on the *stability* and *lack of side effects* of *tannate* salts, and Kupper's commending of *pharmaceutically acceptable salts*, to further substitute carbetapentane *tannate* for Kupper's dextromethorphan *HBr*—the Examiner asserting that the Kupper salt teaching would support an *expectation of similar results*.

Again the Examiner's approach in *this* rejection is to pick and choose isolated teachings from the references, ignore *the whole* of each reference, and then string the isolated piecemeal teachings into an attenuated *non-sequitur* that the artisan would **not** have made. In response to this infirm analysis, Applicants can just as easily string *less* attenuated teachings from the references in such a way as to rebut the Examiner's motivation arguments:

First, carbetapentane is an *antitussive* (Denick, col. 4, lines 1-3), not an *antihistamine* (Denick, col., lines 4-7) as Chopdekar mischaracterizes it to be (col.3, lines 1-10. Chopdekar is entitled: *Process for Preparing **Antihistamine** Tannates* (emphasis added); and its *Abstract*, rife with reference *only* to "antihistamine," would motivate the Kupper-informed artisan, looking for *antitussive* instruction, to ignore Chopdekar entirely, thereby depriving himself of the tannate "stability" and "side effects" tangents

[1] Carbetapentane is an *antitussive*, not an *antihistamine*.

that are so critical to the Examiner's *tannate* motivation road map.

Second, assuming that the Kupper-informed artisan *would* have read Chopdekar anyway *and* made both the free base substitution *and* the tannate salt substitution, neither of those substitutions is suggested or supported by Kupper or by the knowledge generally available to those of ordinary skill in the art. This is because Kupper's *pharmaceutically acceptable organic salt* teachings do not commend *tannate* salts, *tannic* acids, or *tannins* of any kind:

> "**Salts derived from pharmaceutically acceptable organic non-toxic bases include** salts of primary, secondary, tertiary and quaternary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as triethylamine, tripropylamine, 2-dimethylaminoethanol, 2-diethylaminoethanol, lysine, arginine, histidine, caffeine, procaine, N-ethylpiperidine, hyrdabamine, choline, betaine, ethylenediamine, glucosamine, methylglycamine, theobromine, purines, piperazine, piperidine, polyamine resins and the like." (page 4, lines 13-20, emphasis added).

That conclusion also obtains because the art does not consider *hydrobromides* and *tannates* to be interchangeable *functional equivalents.* Therefore the artisan would **not** substitute carbetapentane tannate for the dextromethorphan HBr in Kupper's *Example II.* It is well known in the art that *tannate salts* of active ingredients tend to be slow dissolving and slow delivering. (See page 1, *The Eclectic Materia Medica, Pharmacology and Therapeutics*; *GRANATUM*; attached hereto as Exhibit A). As a result, Cmax is achieved at a later time. In contrast, it is equally well known in the art that *hydrobromide salts* of active ingredients are fast dissolving and fast delivering, whereby C_{max} is reached in a shorter time period. (See page 3, *Rapifilm – Rapid Release Dosage Form*, by Mertin, of Labtec GmbH; attached hereto as Exhibit B). As these well-known delivery disparities are not insubstantial differences, the artisan of ordinary skill,

contrary to the Examiner's assertions, would **not** have expected similar results after substituting carbetapentane *tannate* for Kupper's dextromethorphan *HBr*. Clearly then, the dextromethorphan *HBr* of Kupper, and the claimed carbetapentane *tannate* (which is not exemplified in either reference), are **not** functional equivalents as the Examiner contrives to suggest them as being.

The ease with which such a rebuttal can be similarly strung underscores the importance of considering each reference *as a whole*, rather than a bunch of isolated statements from which the Examiner may selectively assemble any argument she chooses. Such an approach is tantamount to giving the Examiner license to ignore those of the reference's teachings that would undermine the Examiner's arguments.

While the above piecemeal analysis adequately rebuts the Examiner's piecemeal arguments, a more precedent sound traverse for the combination's want of *motivation* is the analysis that the Examiner strives to avoid, succinctly: considering the invention *as a whole*, in view of *the whole* of each reference's teaching—rather than just selectively culling from the art isolated differences to thereby support a conclusion of unpatentability. After all, the question under 35 U.S.C. § 103 is not whether the *differences* between the claims and the prior art would have been obvious, but rather, whether the claimed invention *as a whole* would have been obvious. Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530 (Fed. Cir. 1983). This determination requires that the prior art *also* be considered *as a whole*—in its entirety. W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540 (Fed. Cir. 1983).

It is well-known in the art that guaifenesin is generally dosed as an immediate release formulation. Indeed, there is only one FDA-approved extended release

guaifenesin formulation currently on the market and it is a single active ingredient formulation. (See *FDA Orders Most Long-Acting Guaifenesin Products Off The Market*; Pharmacist.com; attached hereto as Exhibit C). More importanty, the claimed invention *as a whole* is the novel and nonobvious combination of the *immediately releasing* expectorant, guaifenesin, and the *extendedly releasing* antitussive, carbetapentane *tannate*:

> "The compositions described herein are designed to be taken twice a day with the **immediate** expectorant action of guaifenesin and the **prolonged** antitussive action of carbetapentane tannate." (Specification page 3, para. 4; emphasis added).

There is nothing in any of the references that suggests the combination of an immediate release expectorant in combination with an extended release antitussive, in general, and much less is there any suggestion that would commend guaifenesin in combination with carbetapentane *tannate* as claimed, in particular. The Examiner's reliance upon Kupper's *Example II* contains no such suggestion, because dextromethorphan HBr is known in the art to be an immediate release active ingredient, just like the guaifenesin that Kupper pairs it with. The Examiner's assertion that dextromethorphan, as an antitussive, is the "functional equivalent" of carbetapentane selectively ignores the fact that Kupper's *Example II* doesn't teach dextromethophan, it teaches dextromethophan HBr, which, owing to its immediate release properties, is clearly **not** a "functional equivalent" of the claimed carbetapentane *tannate*.

And, even if Kupper's dextromethorphan **HBr** *was* the functional equivalent of the claimed carbetapentane **tannate**, which it is not, the *functional equivalency* of a claim *as a whole* is not the test for obviouness, and much less is the *functional equivalency* of a *single claim element* found in the art the appropriate test for obviousness. The late Judge

Rich explained it succinctly forty years ago:

> "The defect which we find in the reasoning employed below to support the rejection here is not only that it ignores the express provision of the statute as stated is section 103 but that it also ignores the fact that **it is advantageous to the public in the promotion of progress of the useful arts, the Constitutional objective of the patent law, to provide inducement for the invention of devices which are the functional equivalents of devices already known**. It is not the object of the policy behind the patent system to encourage satisfaction with or commercialization only of the first device for performing a given function that happens to come along. And for those who may be interested in promoting competition in the interest of the consuming public, **the greater the number of functionally equivalent devices which are encouraged onto the market by patent protection, the better off the consumer will be. Therefore the test is obviousness of the invention and not whether it serves the same purpose as previous inventions**." Application of Flint, 51 C.C.P.A. 1230, 1235-36 (CCPA 1964)(Applicant's emphasis added).

Judge Rich's admonishment could not have greater relevance than to the cough / cold formulation arts, wherein the variation of consumer choice is a function of the obsolescences dictated by each successive cold and flu season. Clearly, whatever "functional equivalency" dextromethorphan may have with carbetapentane, or any other antitussive, that "functional equivalency" does not render the claimed combination obvious.

The teachings of the art must be similarly considered *as a whole*. Kupper *on the whole*, like Denick *on the whole*, teaches the artisan how to mask the unpleasant taste of known active ingredients. That Kupper "by itself" could render the instant claims obvious is preposterous, since the artisan would only turn to Kupper for taste masking instruction. In other words, the artisan's resort to Kupper, in the first instance, presumes that s/he has already chosen the active ingredient, and that that active ingredient is necessarily a harsh tasting ingredient that needs taste masking. As Aida informs,

carbetapentane *tannate* is not a harsh or bitter tasting active, and therefore the artisan having decided to use it as his antitussive would have no reason to turn to Kupper, in the first instance. On the other hand, the artisan having chosen dextromethorphan *HBr* as his antitussive *might* have turned to Kupper for taste masking instruction, because unlike carbetapentane *tannate* the art recognizes that dextromethorphan **is** a harsh tasting active. (See page 8, *South Carolina Drug Threat Assesment: Other Dangerous Drugs*; National Drug Intelligence Center December 2001; attached hereto as Exhibit D):

> "Some users ingest DXM directly from the bottle, but others, trying to minimize the **unpleasantness of the flavor**, heat the liquid to crystallize the substance. Law enforcement agencies report that many young people who tried abusing DXM once resist using it again due to the **bad taste** and unwanted side effects, such as headaches, nausea, and vomiting." (emphasis added).

Thus, the artisan using carbetapentane tannate, knowing it **not** to be harsh tasting, would **not** be guided to Kupper.

Chopdekar, *on the whole*, teaches a *Process for **Preparing** Antihistamine Tannates*—a process which Aida predates with regard to carbetapentane specifically, by thirty-three years. (Compare the seemingly identical methods of Aida and Chopdekar). Chopdekar teaches the artisan how to **make** an anti***histamine*** tannate; it teaches the artisan nothing about the desirability *vel non* of mixing an anti***tussive*** with any other active class of drug. Additionally, the artisan having in Aida a methodology for making a tannate salt, *specifically* carbetapentane, would have no reason to look to Chopdekar, a reference that teaches how to make ***antihistamine*** tannate salts *generally*. Lesser still would the Aida-informed artisan, cognizant of carbetapentane tannate's palatability, have any reason to consult a taste masking reference such as Kupper. Accordingly, upon weighing the suggestive power of each reference as a whole (MPEP 2143.01) the artisan

would have no motivation to consult either Kupper or Chopdekar, and therefor both Kupper and its proposed combination with Chopdekar are traversed.

Claims 15-30 Are Not Obvious Over Kupper By Itself, Nor In View Of Chopdekar In Further View Of Sims

Claims 15-30 are narrowed versions of the previously discussed claims wherein the odd numbered claims are each independent, having elements drawn to ranges of active ingredients. And each even numbered claim is dependent on its predecessor, having elements drawn to specific amounts of active ingredients. Claims 23-30 are further narrowed by having elements drawn to twice-a-day (BID) dosing.

The Examiner repeats each of the arguments of the preceding section regarding Kupper and Chopdekar, conceding *only* that these combined references do not teach the dosage range of the antitussive.[2] To remedy this concession the Examiner offers Sims, a patent directed to *Ibuprofen-Antitussive Combinations* that was previously relied upon as the *sole* reference to support earlier rejections of the claims.

The Examiner selectively notes, as she did with Chopdekar, that carbetapentane is among the five antitussives that Sims discloses as being essential to the Sims invention. (col. 1, lines 38-43). With greater selection still, the Examiner notes that *tannates* are *specifically* listed among the salts that Sims commends for use with his antitussive Markush group. Sims notes, and the Examiner ignores, that the nine *specifically* listed salts are not limited thereto. (col. 2, lines 37-39).

To meet the dosage amounts of the instant claims, the Examiner next asserts that

[2] The Examiner fails to repeat her concession that Kupper does not exemplify carbetapentane tannate.

Sims teaches that "[t]he antitussive is utilized in the amount of 1-50 mg depending on the specific antitussive used and the expectorant in the amount of 100-1000 mg." Again the Examiner's approach is to selectively parse Sims' language and to ignore Sims' teaching *as a whole*. Indeed, even the Sims language relied upon by the Examiner is not considered *as a whole*. With regard to active ingredient amounts Sims offers that:

> "The antitussive employed herein is selected from codeine, hydrocodone, carbetapentane, caramiphen, and dextromethorphan, or a therapeutically active stereoisomer thereof substantially free of its other stereoisomers, or a pharmaceutically acceptable salt thereof.
>
> **The amount of antitussive useful in the practice of the present invention may vary from about 1 mg to 50 mg depending on the specific antitussive**. **The amount of a salt** such as codeine phosphate **is determined based on the amount of antitussive contained therein**. The amount of expectorant useful in the practice of the present invention may vary from about 100 mg to 1000 mg per daily dosage." (col. 3, lines 24-39, emphasis added).

It is clear from the above Sims excerpt that, contrary to the Examiner's assertion, the amount of the antitussive taught therein is not "the suitable and conventional range of the cough agents in cold remedy formulations." Rather, the antitussive amounts taught in Sims are those amounts of specific antitussives that are necessary to give rise to the potentiated and synergistic relationship that Sims discloses between the *S*-enantiomer of ibuprofen and any of Sims' five specific antitussives.

As a whole, Sims teaches the artisan *only* that it is desirable to combine an analgesic with an antitussive. More specifically, Sims teaches the artisan that it is desirable to combine the S-enantiomer of ibuprofen with one of several specific *antitussives*. The desirability of that combination is clear from Sims' laudatory rhetoric regarding the improved pain relief advantages that ibuprofen's *S*-enantiomer brings to

antitussive combinations, over racemic ibuprofen formulations:

> "The utilization of (S)-ibuprofen in an analgesic/antitussive combination offers significant advantages over the combination of racemic ibuprofen with an antitussive. (S)-ibuprofen provides a faster onset of pain relief and an enhanced degree of relief compared to racemic ibuprofen. These benefits are increased in an (S)-ibuprofen/antitussive combination as **the antitussive may potentiate the action of the (S)-ibuprofen**. This has not heretofore been observed because the art has not proposed the combination of the (S)-ibuprofen enantiomer, absent (R)-ibuprofen, with an antitussive. **Furthermore the antitussive also may potentiate the duration of the analgesic and anti-inflammatory response. The presence of the (R)-ibuprofen may blur the potentiated effect**." (column 2, lines 46-59, emphasis added).

Clearly, the antitussive ranges that Sims discloses are directed to ranges that the artisan would rely upon *only* in his efforts to potentiate and enhance the analgesic effects of S-ibuprofen. They are **not** directed to ranges that the artisan should rely upon, with a reasonable expectation of success, in his efforts to formulate a cough / cold composition, as claimed. Such conclusion is unavoidable in view of Sims' own admonishment that "[t]he amount of a **salt** such as codeine phosphate is determined based on the amount of antitussive contained therein." Accordingly, the 1-50 mg teaching of Sims, which is directed to, and dependent "on[,] the specific antitussive" (col. 3, lines 31-33), does not teach the artisan the independently-claimed *ranges* of the carbetapentane *tannate* salt, and much less the dependently-claimed carbetapentane tannate salt *amounts*.

In his efforts to derive the *twice-a-day* compositions and methods of claims 23-30, the artisan would be the *more* confounded by Sims active ingredient dosage range teachings, because Sims only teaches a *daily* dosage range for his *optional* expectorant and not for his *critical* antitussive:

> The amount of antitussive useful in the practice of the present invention may vary from about 1 mg to 50 mg depending on the specific antitussive. The amount of a salt such as codeine phosphate is determined based on the

> amount of antitussive contained therein. **The amount of expectorant useful in the practice of the present invention may vary from about 100 mg to 1000 mg per daily dosage**." (col. 3, lines 30-39, emphasis added).

Accordingly, Sims teaches or suggests nothing with regard to the *daily* dosage of the antitussive, and much less with regard to the *twice-a-day* dosage of the carbetapentane tannate salt, as claimed in claims 23-30.

The Examiner ignores this shortcoming in the reference, and in regard to the method claims she *deems* it obvious to deliver an entire day's dosage at one time or to divide the dosage into multiple dosages. This supposition is based on the Examiner's assertion that criticality lies only in administering an "effective and maximum" dosage [3], rather than how many times it is administered. With regard to the twice-a-day *composition* claims (23 and 25), the Examiner argues that this element is not given any patentable weight since it appears in the preamble, as an expression of intended use. Without conceding either of the Examiner's arguments, Applicants have amended composition claims 23 and 25 so that the *twice-a-day* aspects of these claims are expressed in the body of the claims, by defining the "pharmaceutically effective amount" aspects in terms of providing BID (twice daily) dosing.

The Examiner's focus upon the "criticality" of dosage being found in the "effective and maximum" dosage has nothing to do with the test for obviousness, which considers the invention *as a whole*. None of the three references here cited by the Examiner even exemplifies carbetapentane tannate, and much less do they collectively suggest its combination with guaifenesin: the Examiner's arguments concerning dosage

[3] There is no case or Board decision cited by the Examiner, making her use of quotation marks confusing.

ranges and amounts presume the contrary. Moreover, the Examiner's assertion that once-daily, twice-daily, or multi-daily delivery of the "effective and maximum" dosage is not critical ignores widespread acceptance by the art that BID, TID, or QID dosing of a particular active is dictated by all manner of considerations (i.e., achieving effective plasma levels, compensating for a particular active's short half-life, ameliorating certain side effects, or delivering several classes of actives in combination)

Moreover, as the twice-a-day aspects of these claims (23-30) embody a daily dosage of carbetapentane tannate that is double the range or amount recited in the claims, each tablet embodiment (23, 24, 27, & 28) and each *dependent* suspension embodiment (26 & 30) provides a daily dosage of the carbetapentane tannate that is in excess of the upper limit of the "1 mg to 50 mg" antitussive range, disclosed by Sims. The Examiner's arguments regarding the criticality of delivering the "effective and maximum" daily dosage are therefore traversed by both the amendments to the claims and Sims' failure to teach an antitussive range that suggests the claimed BID dosing ranges and amounts.

Accordingly, the references, whether considered alone or collectively, do not teach or suggest the basic carbetapentane tannate and guaifenesin combination. Nor do they teach or suggest that combination in tablet or suspension form in further combination with the ranges, amounts, or BID dosing elements that further define additional embodiments of the instantly claimed invention.

In view of the foregoing, Applicants submit that the claims are patentable in view of the cited references. As the application is in all respects in condition for allowance,

Applicants request its prompt passage to issue.

It is believed that no fee is due. However, if any fee is due it should be charged to Deposit Account No.: 03-0678.

CERTIFICATE OF MAILING

Deposit Date: March 24, 2004

I hereby certify that this paper and the attachments hereto are being deposited today with the U.S. Postal Service with sufficient postage as First Class Mail to Addressee, under 37 CFR 1.8, on the date indicated above addressed to:

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3/24/04

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The Eclectic Materia Medica, Pharmacology and Therapeutics.

by Harvey Wickes Felter, M.D., 1922.

GRANATUM.

Other tomes: Cook - Ellingwood - Petersen - BPC - Sayre - King's

The dried bark of the stems and roots of *Punica Granatum*, Linné (Nat. Ord. Punicaceae). India, southwestern Asia, and the Mediterranean shores; naturalized and cultivated in warm latitudes. *Dose*, 30 grains.
Common Names: Pomegranate, Pomegranate Root Bark.

Principal Constituents.—*Pelletierine* or *punicine* (1/2 per cent), methyl-, pseudo-, and isopelletierine, all alkaloids, and punico-tannic acid (20 per cent).
Preparations.—1. *Pelletierinae Tannas*, Pelletierine Tannate. (Contains in varying proportions, in admixture, the four alkaloids mentioned above.) A pale-yellow, noncrystalline powder, without odor, and an astringent taste. Soluble in alcohol and less readily in water. *Dose*, 4 grains.
2. *Decoctum Granati*, Decoction of Pomegranate Bark (see below).
Specific Indications.—Taeniacide and taeniafuge for the destruction and expulsion of tapeworm.

Action.—Pomegranate preparations, in large doses, causes nausea and vomiting, flatulence and intestinal pain. Notwithstanding the large amount of tannin it contains, such action is frequently followed by diarrhea. Other effects are tremors, muscular weakness, and cramps in the extremities, dizziness, mental confusion, drowsiness, diplopia and mydriasis, and other ocular disturbances. The tannate kills the tapeworm easily, but has far less effect upon other intestinal parasites. The associated alkaloids, sold as pelletierine, constitute an exceedingly active combination, capable of producing paralysis of the motor nerves. The tannate, probably owing to its slow solubility, is less liable to disturb the system, but is equally effective as a taeniacide.

Therapy.—When pomegranate decoction can be retained by the stomach it is a certain specific for the destruction and expulsion of tapeworm. When this preparation cannot be used, the tannate, which is far more easily administered, may be substituted. A semi-proprietary preparation called "granatin" is a salt of pelleterine in solution, and is a very effective destroyer. It is sold ready for administration as a single dose. Locke's method of treating tapeworm is popular with Eclectic physicians. The decoction he advised is prepared as follows: Press 8 ounces of the coarse bark into a vessel and pour upon it three pints of boiling water; boil, strain, and then boil again until but one pint remains. A brisk cathartic should be given at night and a light breakfast allowed in the morning. In the middle of the forenoon four ounces of the decoction should be administered. In order that this may pass quickly into the intestines and its absorption be prevented, as far as possible, a fluidrachm of fluidextract of jalap aromatized with oil of anise or oil of cinnamon should be given with the dose. In two or three hours the dose should be repeated. When the bowels begin to move administer a copious enema, and remove the worm in a vessel filled with warm water so that it may float freely and not be broken. If nausea and

vomiting occur upon first giving the decoction, lemon juice should be given and the recumbent position maintained.

When pelletierine preparations are administered a light milk diet in the evening is followed in the morning by a saline purge, and then the combined alkaloids administered. In about one hour another dose of the purgative should be given. Epsom salt, fluidextract of jalap, or castor oil may be used as the cathartic. If the tannate is employed it may be administered in capsule.

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Rapifilm - rapid release dosage form

Dr. Dirk Mertin,
Labtec GmbH

2 The Technology of Rapifilm

1.1 General description

Peroral application is an effective and reasonable delivery route for drugs, which can be absorbed in the gastro-intestinal tract. However, sometimes the application of tablets or liquids is difficult:

- Normally a tablet has to disintegrate, before the active ingredient can dissolve. Both processes delay more or less the onset of action, which is undesirable in some diseases or symptoms, such as pain.

- Patients suffering from gastro-intestinal diseases are often not able to swallow solid dosage forms due to nausea. In the past this problem was solved by the application of liquids. However, the drug dosing by counting of drops or by a measuring spoon is time-consuming and not very precise. Moreover, some drug are not stable in aqueous or alcoholic-aqueous solutions.

- Sick children often resist the application of drugs. Tablets are spit out, liquids are spilled due to the strong agitation of the little patients.

Rapifilm combines the advantages of tablets (exact drug dosage) and those of liquids (easy swallowing, rapid drug bioavailability).

+ The film dissolves immediately after oral intake and releases the drug. Dependent on its physicochemical properties a considerable amount of the drug can be absorbed by the oral mucosa. Even in case of immediate swallowing of the resulting drug suspension or solution the increase of plasma levels is faster than with fast release tablets.

+ As the patient swallows a drug suspension or solution there is no lump sensation in the throat. The system ensures a good patient compliance even in the case of disorders causing sickness. Spitting out the dosage form is not possible, because the film adheres slightly to the oral mucosa before dissolving. Thus, the safety of drug application to children is considerably improved.

+ As Rapifilm is a single dose application, the dosage uniformity is guaranteed in contrast to liquids.

1.2 The System

Rapifilm is a thin, drug containing film with an area of 5 to 10 cm^2. The rapid dissolution in water or salvia is ensured by a special matrix of water-soluble polymers. Drugs can be added up to a single dose of 15 mg. A typical formulations contains the following substances:

- Drug(1 - 25 %)
- Water-soluble polymers(40 - 50 %)

- Softener(0 - 20 %)
- Fillers(0 - 40 %)

Only pharmaceutically accepted polymers like cellulose ethers (HPMC, HEC and MC), PVP, PVA or gelatine are used. An unpleasant taste can be masked by the addition of flavours and/or sweeteners.

The primary packaging is made of a sealing pouch, which affords enough space for logos, codes, instructions or other informations.

1.3 Manufacturing

Conventional rapid release dosage forms like ZydisÒ (R.P. Scherer) are manufactured by lyophilisation of a drug containing solution or suspension. However, this established technology is time and cost consuming, thus it is only suitable for expensive pharmaceutical products.

In contrast to that Rapifilm is manufactured by a laminating process, well-known from the production of transdermal systems for a long time. A drug containing solution or suspension is coated on a release paper or foil. The solvent, preferably water or water-alcohol mixtures is evaporated, the resulting laminate is punched and finally packed in a peel blister. Fig. 1 shows the scheme of a typical coating machine:

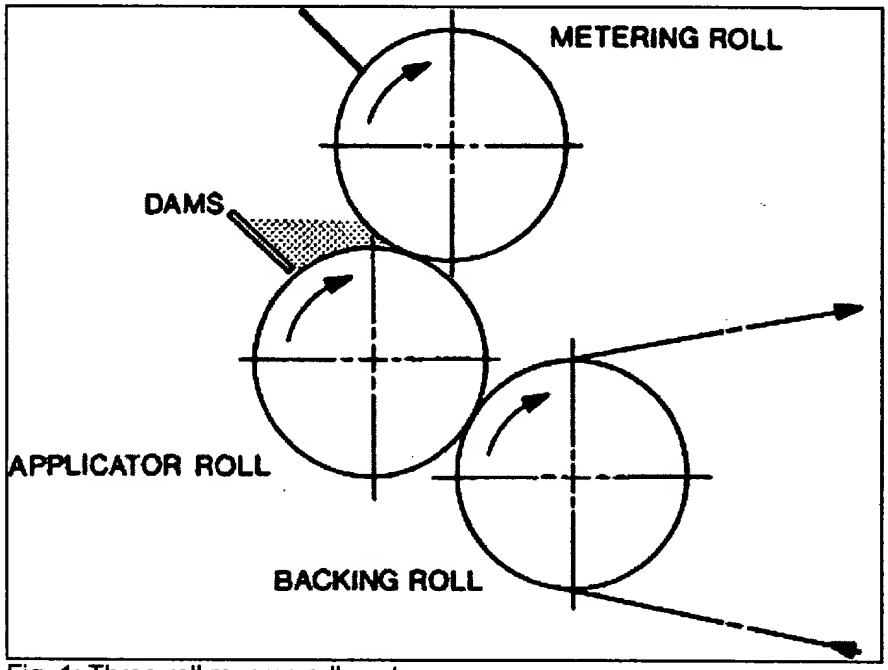

Fig. 1: Three-roll reverse roll coater

The manufacturing costs for a package with two blisters (10 units each) are in the range of € 0.60 (without drug). The production by a manufacturer, which has much experience with pharmaceutical coating processes, is ensured by long-term contracts.

1.4 Drug release

In order to guarantee an immediate drug dissolution in the oral cavity
a) the drug has to be sufficiently water-soluble and
b) the dosage form has to disintegrate rapidly.

If the drug has a poor water solubility and is not available as a water-soluble salt, a rapid disintegration of the film is an important condition for a fast drug absorption from the gastro-intestinal tract.

Formulations with the drug substances ambroxol hydrochloride, dextromethorphan hydrobromide, metoclopramide hydrochloride, ketotifen hydrogenfumarate, loperamide hydrochloride were developed and their in-vitro dissolution was tested (Ph. Eur., rotating basket). These studies show that the drug is released completely within 2 to 3 minutes (Fig. 2). This exceptionally fast dissolution allows mucocutaneous absorption before swallowing the drug solution, if the film is applied at a suitable place (e.g. under the tongue). This means a rapid increase of plasma levels and a fast onset of action.

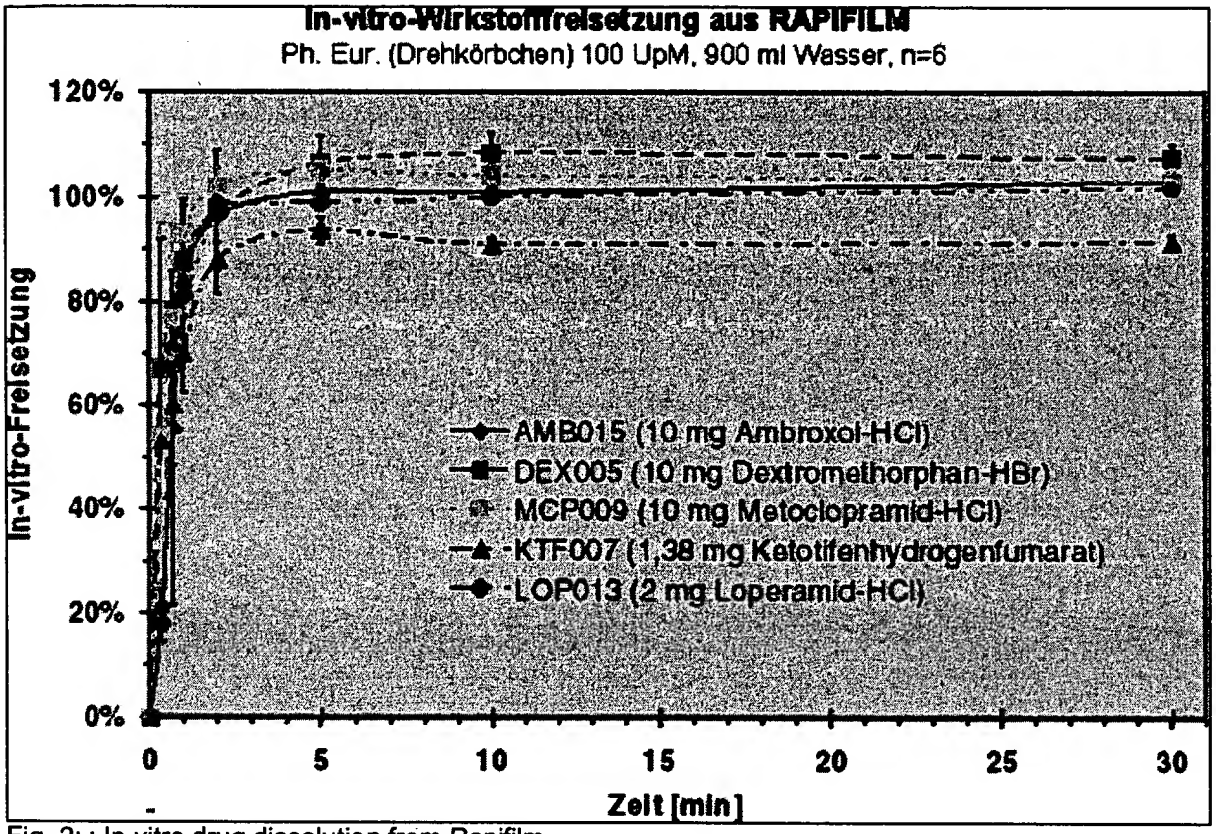

Fig. 2: : In-vitro drug dissolution from Rapifilm

Moreover, the drug dissolution should be independent of the pH value. A pH of 6 to 7 in the oral cavity determines the dissolution in the salvia, whereas the pH of the stomach is between 1 and 3. The drug amount dissolving in the oral cavity and in the stomach respectively is dependent on the swallowing rate. Therefore, the drug dissolution must be sufficiently high in both media.

Fig. 3 shows the in-vitro release of loperamide from Rapifilm and from a commercial, rapid dissolving product (ImodiumÒ lingual, dosage form ZydisÒ) in 0.1-N hydrochloric acid (pH corresponding to gastric juice) and water (pH corresponding to salvia). Whereas Rapifilm releases the drug within five minutes completely and independently of the pH value, the dissolution of loperamide in water from the commercial product is sustained. In this case the drug can not be absorbed by the oral mucosa but only after reaching the gastro-intestinal tract when the drug suspension is swallowed. In contrast to that, the drug dissolves in the salvia after the application of Rapifilm and can be absorbed immediately by the buccal mucosa.

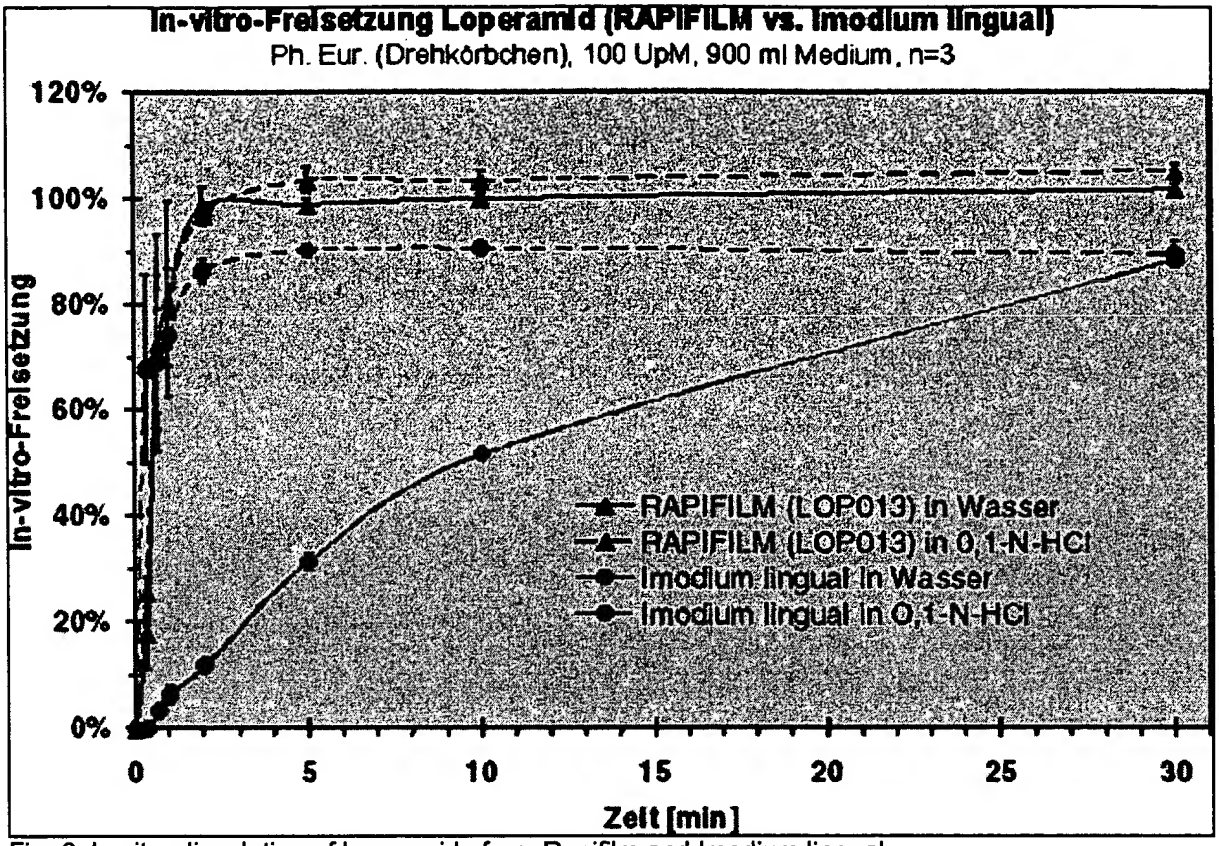

Fig. 3: In-vitro dissolution of loperamide from Rapifilm and Imodium lingual

By means of the innovative delivery system Rapifilm a very fast release of many drug substances can be obtained, which is independent of the pH value of the dissolution medium. Moreover, there is a clear cost advantage over the established technology of lyophilisation.

1.5 Patent Status, Know-how

A patent application for the manufacturing of Rapifilm was filed at the German Patent Office in October 1998 (DE 19745208). The know-how of Labtec results in the fast development and reasonable production of formulations. The costs of manufacturing are able to compete with conventional single-dose, solid dosage forms like tablets.

2 Cooperations with pharmaceutical companies

A couple of innovative drug products can be developed by means of this base technology. The properties of Rapifilm can be utilized with the following indications:

1. Application to patients, which have difficulties in swallowing solid dosage forms
   - Children: Ambroxol and dextromethorphan are indicated in the therapy of respiratory diseases. Ketotifen is often used for the treatment of juvenile asthma.
   - Geriatric patients: Difficulties in swallowing often occur in Parkinsonism. Possible drugs are selegiline or dopamine agonists, like bromocriptine, pergolide or lisuride.
   - Patients, which are suffering from nausea: Metoclopramide in the case of motility disorders and migraine, the novel "setrones" in the case of nausea caused by cytostatic drugs and H2-antihistaminics in the case of gastritis and heartburn.
2. Situations, in which a fast onset of action is desired
   - Pain (especially migraine): A fast onset of action is necessary in the case of a treatment with ergotamine or modern serotonine agonists ("triptanes"),
   - Sleeping disorders: Especially in the case of difficulties to fall asleep short-acting

benzodiazepines, zopiclone and zolpidem are used.

Therefore, the technology of Rapifilm can be used for the development of innovative dosage forms of well-known and approved drugs. The investment for the pharmaceutical development is considerable. The clinical studies requested for approval have to be calculated according to the type of product (generic/NCE). An existing approval for a fast release tablet, which is available on the market, can be used after performing a small bioequivalence study. Especially medium-sized pharmaceutical companies can develop innovative products of generic or own drug substances by means of this technology. Rapifilm is also suitable to give a new input to substances or brands, which loose their patent protection in the near future (line extension).

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TOP STORIES - ARTICLE

FDA orders most long-acting guaifenesin products off market

Only Adams' Mucinex product currently approved; other manufacturers have until end of November to distribute 'illegal' products.

Last October, FDA issued warning letters stating that single-ingredient extended-release guaifenesin products are new drugs and require an approved new drug application for legal marketing under the Federal Food, Drug, and Cosmetic Act. The only approval, issued in July 2002, is for guaifenesin 600 mg extended-release tablets from Adams Laboratories.

In the warning letters, sent to 66 manufacturers, FDA stated that its actions "reflect the Agency's effort to maintain the necessary incentives for companies to develop and submit to FDA scientific evidence to prove the safety and effectiveness of marketed drug products."

FDA also intends to publish a notice in the Federal Register about its policy on unapproved drugs. In a talk paper posted to the FDA Web site, the agency explained that it reviewed products in this category after approving the Adams' product last July, and it concluded that products with unproven safety and effectiveness should not remain on the market when an approved product had become available. This preserves the incentives for companies to develop and submit new drug applications, as required by law, FDA added.

Guaifenesin's main use is for productive coughs. It is the only FDA-approved nonprescription expectorant. As a pre-1962 product, its effectiveness has never been well established, but it causes few adverse effects and is commonly included in many cough-and-cold products. As part of FDA's review of OTC products, immediate-release guaifenesin was previously ruled to be safe and effective.

Web links
Guaifenesin monograph: APhA members can access Lexi-Drugs Online from the Drug Information section of pharmacist.com
FDA [http://www.fda.gov/bbs/topics/ANSWERS/2003/ANS01201.html]
Special Report: Self-Care of the Common Cold in Pediatric Patients [http://www.pharmacist.com/pdf/common_cold_sr.pdf]
Special Report: Solving Drug Therapy Problems in Patients With Allergic Rhinitis [http://www.pharmacist.com/pdf/solving.pdf]

Contact the writer: Suzanne Price (sprice@aphanet.org), Pharmacy Today

Updated February 28, 2003 10:24 am EST

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National Drug Intelligence Center
South Carolina Drug Threat Assessment
December 2001

Other Dangerous Drugs

The other dangerous drugs (ODD) category includes club drugs, hallucinogens, and illegally diverted pharmaceuticals, in addition to household products and over-the-counter medications abused mostly by youth.

Club Drugs

Other dangerous drugs include those classified as "club drugs." Club drugs are used by teens and young adults at all-night dance parties called raves that are generally held in clubs in cities and beach resorts in South Carolina. Raves feature loud music, flashing light displays, and often extensive drug use. Some club drugs are MDMA (3,4-methylenedioxymethamphetamine), LSD (lysergic acid diethylamide), GHB (gamma-hydroxybutyrate), Rohypnol (flunitrazepam), and ketamine. These drugs run the gamut from stimulants to sedatives to hallucinogens. Local law enforcement agencies in South Carolina report increases in the popularity of club drugs in the larger metropolitan areas and in some beach communities. However, low levels of abuse are reported throughout the rest of the state. Club drugs primarily are distributed by Caucasian criminal groups and local independent dealers.

GHB and GBL

Of the club drugs available in South Carolina, GHB poses the greatest threat. GHB, also known as liquid ecstasy, scoop, grievous bodily harm, and Georgia home boy, is abused for its euphoric, sedative, and anabolic effects. However, use can induce coma and cause insomnia, anxiety, tremors, and sweating. When GHB is combined with methamphetamine, there is an increased risk of seizures. Overdoses can occur quickly; some of the signs include drowsiness, nausea, vomiting, loss of consciousness, and impaired breathing, and even death. The drug increasingly is involved in poisonings, overdoses, date rapes, and fatalities nationwide, including South Carolina. GHB can be made from easily obtainable ingredients such as GBL (gamma-butyrolactone), a solvent commonly used as a paint stripper, or butanediol (1,4-butanediol), a chemical used in the production of plastics and adhesives. Both GBL and butanediol are metabolized into

GHB in the body. GHB, GBL, and butanediol are difficult to trace because they quickly leave the body and may be difficult to detect in emergency rooms and other treatment facilities. In South Carolina, during 2000, distributors could purchase GHB illegally for $400 a gallon, and users could purchase GHB illegally for $5 to $20 per dose.

Law enforcement agencies report incidents of GHB abuse and distribution in South Carolina.

Greenville area hospitals in western South Carolina reported weekly occurrences of GHB overdoses, and the county coroner confirmed two deaths due to GHB overdoses in 2000.

In 2000, three Virginia men were convicted of producing and distributing GHB in Myrtle Beach. The defendants testified that they used GHB to get high and because they believed it increased muscle mass.

In 2000, a Charleston medical student received 500 milliliters of GHB from a relative in Iowa via a package delivery service. When arrested, he told police he intended to treat two women who were suffering from illness and depression.

GBL, sometimes called liquid ecstasy, a controlled chemical used in the production of GHB, is a widely available industrial strength commercial cleaner used as a solvent in floor and furniture stripping as well as in engine cleaning. On January 21, 1999, the Food and Drug Administration (FDA) issued a warning about food supplement products containing GBL and requested that producers recall all products containing the additive. According to a January 2000 report, GBL has been implicated in at least six deaths nationwide. GBL is sold in powdered and liquid form at gyms, fitness centers, and some health food stores. GBL is a precursor used to make GHB, and produces similar effects. Once ingested, GBL metabolizes into GHB.

Law enforcement agencies in South Carolina report incidents of GBL abuse across the state.

In 2000, a 21-year-old Greenville man drank a soda bottle cap full of "home brew" after which he collapsed into a seizure and nearly died. He later discovered the substance was "Blue Nitro," a common name for GBL.

In 2000, two Charleston brothers sold "date rape" drug kits--disguised as computer-cleaning solvents--on their web site. The $55 kits consisted of enough GBL and sodium hydroxide to make 15 to 20 doses of GHB. Police seized a 55-gallon drum of GBL and 10 pounds of sodium hydroxide from the brothers' home.

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MDMA

MDMA, also called ecstasy, XTC, E, X, or Adam, is a synthetic psychoactive drug with amphetamine-like and hallucinogenic properties. MDMA was patented in Germany in 1914 and sometimes was given to psychiatric patients to assist in psychotherapy. The American Psychological Association or the FDA never approved this practice. Users say MDMA, sometimes called the "hug drug," makes them feel good. However, the drug may cause psychological difficulties similar to those associated with methamphetamine and cocaine abuse including confusion, depression, sleep problems, anxiety, and paranoia. The physical effects include muscle tension, involuntary teeth clenching, blurred vision, and increased heart rate and blood pressure.

Taken in high doses, MDMA can be extremely dangerous. It can cause a marked increase in body temperature, leading to muscle breakdown and kidney and cardiovascular system failure. MDMA use may lead to heart attack, stroke, and seizure, as reported in some fatal cases at raves. Recent research links MDMA to long-term, possibly permanent, damage to parts of the brain that are critical to thought and memory. There is also evidence that individuals who develop a rash after using MDMA may suffer severe liver damage or other serious side effects.

According to DEA estimates, about 80 percent of the MDMA consumed worldwide is produced in laboratories in the Netherlands and Belgium. While much of the MDMA in South Carolina is transported from other states, some local independent distributors are producing the drug. In 1999, DEA seized three MDMA laboratories in Charleston County.

MDMA distribution and use are most prevalent in the metropolitan and tourist areas of South Carolina. Local independent dealers dominate the retail distribution of MDMA. They travel to Atlanta, Charlotte, New York, Washington, D.C., and cities in Florida to purchase MDMA and transport it back to South Carolina. Dealers can purchase MDMA at the wholesale level for $12.50 a pill. Teenagers and young adults purchase MDMA at raves, nightclubs, or from retail distributors, generally between $20 and $30 per dose.

LSD

LSD, also known as acid, boomers, and yellow sunshines, is a

hallucinogen that induces abnormalities in sensory perceptions. The effects of LSD are unpredictable depending on the amount taken, the environment in which it is used, and the user's personality, mood, and expectations. Users may feel the effects within 30 to 90 minutes. The physical effects include dilated pupils, higher body temperature, increased heart rate and blood pressure, sweating, loss of appetite, sleeplessness, dry mouth, and tremors. LSD users report numbness, weakness, or trembling, and nausea is common. Two long-term disorders associated with LSD are persistent psychosis and hallucinogen persisting perception disorder (flashbacks).

LSD is available in many forms, and law enforcement agencies report that its abuse and availability in South Carolina are increasing, primarily among high school and college aged youth frequenting rave parties and clubs. LSD is available as a powder or liquid and is found in tablets and capsules, on pieces of paper that absorb the drug, on small candies, or as microdots. Some users hide the powder or liquid in tiny breath mint vials. LSD typically is taken by mouth, but officials in South Carolina report some users administer the drug by dropping liquid LSD from breath mint vials directly into the corners of their eyes. The SLED reported an increase in the amount of LSD seized from FY1997 (1,470 dosage units) to FY1999 (8,235 dosage units). In South Carolina, a 1,000-dosage-unit blotter sheet sells for $1,500 and a 100-dosage-unit blotter sheet costs $300. The price of a single dose of LSD is $25.

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Rohypnol

Across South Carolina, teenagers and young adults abuse Rohypnol (flunitrazepam) as a club drug and as a date rape drug. Also called roofies, rophies, Roche, and the "forget-me pill," Rohypnol belongs to the class of drugs known as benzodiazepines, but is not approved for prescription use in the United States.

In South Carolina, law enforcement reports that teenagers and young adults sporadically abuse Rohypnol along with other club drugs. Rohypnol is odorless, tasteless, and dissolves in liquid. It can cause severe retrograde amnesia. Rohypnol produces sedative-hypnotic effects including muscle relaxation and amnesia, and can also cause physiological and psychological dependence. The effects of Rohypnol can impair or incapacitate a victim for 8 to 12 hours, and are exacerbated by the use of alcohol. In 1998 the manufacturer changed the formula, adding blue dye and making it more difficult to dissolve so that intended victims of sexual assault could detect the drug in a drink more easily, but these changes are discernible only in transparent containers.

Ketamine

Ketamine abuse is currently a minor problem in South Carolina because its use has decreased since August 1999, when the federal government classified it as a Schedule III drug. Ketamine, also called K, special K, vitamin K, and cat valium, is an anesthetic that has been approved for both human and animal use. It is available in liquid, powdered, or pill form, and as a powder is often snorted or smoked with marijuana or tobacco products. The effects of ketamine are similar to those of PCP (phencyclidine) or LSD, but much less intense. At high doses, it can cause delirium, amnesia, impaired motor function, high blood pressure, depression, and potentially fatal respiratory problems. Low-dose intoxication from ketamine results in impaired attention, learning ability, and memory. Short term use causes hallucinations. During 2000, a vial of ketamine could be purchased for $80 in South Carolina.

Diverted Pharmaceuticals

Pharmaceutical drugs often are diverted in South Carolina. Primarily low-income Caucasian users obtain prescription narcotics and stimulants, as well as many drugs in a class of depressants called benzodiazepines, in a variety of ways. Users may purchase diverted drugs on the retail market or via the Internet from other countries. "Doctor shopping," forged prescriptions, and prescriptions stolen from pharmacies, hospitals, nursing homes, or legitimate users are other ways that users obtain illegal pharmaceuticals. Diverted pharmaceuticals primarily are distributed by Caucasian criminal groups and local independent dealers.

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Narcotics

Hydrocodone and oxycodone, both opium derivatives, as well as methadone, a synthetic narcotic, are the most frequently abused pharmaceuticals in South Carolina.

Hydrocodone is a narcotic that, when combined with acetaminophen (Tylenol) or aspirin, is sold legally under the brand names Lortab and Lorcet. Lortab is sold illegally for $9 a dose, and Lorcet is sold for $5 a dose in South Carolina.

Percocet is a narcotic that contains oxycodone and acetaminophen, and can be purchased illegally for $10 per dose in South Carolina.

OxyContin, the brand name for timed-release oxycodone, is preferred more often than the other diverted pharmaceuticals, but because doctors typically prescribe OxyContin to cancer patients only, it is more difficult to obtain. Individuals obtain OxyContin for sale to retailers by fraudulently obtaining prescriptions from several different doctors. Retailers sell it to users for approximately $25 per pill. State and local agencies see OxyContin distribution and use as a growing problem.

Methadone, commonly used as a treatment for addiction, particularly heroin, can be purchased illegally in South Carolina for $50 per 100 milliliters or $0.65 per milliliter.

Stimulants

Methylphenidate (Ritalin), a stimulant commonly prescribed for the treatment of attention deficit hyperactivity disorder (ADHD), is misused primarily by youth in South Carolina. Law enforcement agencies report cases of legitimate users and other young people crushing the tablets and snorting the drug to experience a high.

Benzodiazepines

Benzodiazepines, including alprazolam (Xanax), diazepam (Valium), and lorazepam (Ativan), frequently are diverted in South Carolina. Law enforcement agencies report that the diversion of Xanax is a problem across the state. Xanax is sold illegally in South Carolina for $6 per tablet and Valium is sold for $3 a tablet. The number of admissions to South Carolina publicly funded treatment centers for benzodiazepine abuse more than doubled from FY1998 (43) to FY2000 (99).

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Others

Young people in South Carolina are using common household products and cough preparations to achieve a high, but the inhalation and ingestion of these over-the-counter products constitutes a serious danger.

Inhalants

Inhalant use, commonly called "huffing," threatens South Carolina's youth. Huffing is the sniffing of common household products such as paint, gasoline, and hair spray. Sniffing these inhalants can introduce toxins into the body and cause damage to the liver, lungs, kidneys, brain, and even death. The number of inhalant users admitted to publicly funded treatment centers has decreased in South Carolina, with 54 admissions in FY1997, 52 in FY1999, and 25 admissions in FY2000.

According to the DAODAS, the primary users of household inhalants are preteens and young teenagers. Adults also use inhalants in South Carolina, but not as frequently as teenagers. Adult users typically have been using inhalants regularly since their teenage years. Young males generally use inhalants more than young females. The majority of these teenagers use inhalants only experimentally or occasionally, and do not become addicted. However, even one use can be dangerous or fatal. According to the 1999 Youth Risk Behavior Surveillance survey, 14.2 percent of South Carolina high school students have used inhalants at least once during their lifetime and 4.1 percent currently use inhalants, compared with 14.6 percent and 4.2 percent nationwide, respectively.

DXM

A recent trend among young people in South Carolina is the misuse of over-the-counter cough suppressants and cold remedies, particularly DXM (dextromethorphan, also called dextro). When users consume DXM in large doses, they may experience hallucinations, impaired motor skills, and behavioral changes. Prolonged use carries the risk of addiction, loss of consciousness, and even death. Some users ingest DXM directly from the bottle, but others, trying to minimize the unpleasantness of the flavor, heat the liquid to crystallize the substance. Law enforcement agencies report that many young people who tried abusing DXM once resist using it again due to the bad taste and unwanted side effects, such as headaches, nausea, and vomiting.

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